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# **Breast-conserving therapy for breast cancer**

## Cosmetic results and options for delayed reconstruction



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## ABSTRACT

**Introduction** Optimizing of the cosmetic outcome after breast conservative therapy (BCT) is important. We aimed to determine the cosmetic outcome following BCT and factors influencing this cosmesis and identify the most favourable options for delayed breast reconstruction.

**Methods** Four reconstructive surgeons evaluated the cosmetic outcome of 109 patients after BCT. Additionally, the surgeons indicated which patients were amenable for delayed reconstruction, and the preferred type of reconstruction. The inter- and intraobserver agreement of the surgeons was rated.

**Results** The mean overall cosmetic outcome was rated as fair (2.7/4.0, SD 0.9, 1.0-4.0). Risk factors for a poor cosmesis were larger breast size (OR 3.81,  $p = 0.040$ ), larger tumour (OR 1.63,  $p = 0.028$ ) and axillary lymph node dissection (ALND) (OR 3.09,  $p = 0.013$ ). Reconstruction of the ipsilateral side was recommended in 55.6% and 94.5% and contralateral reconstruction in 16.7% and 73.3% of patients with good and poor cosmesis, respectively. Flap reconstruction and lipofilling were most commonly reported for the ipsilateral, and breast reduction for the contralateral breast, with reasonable improvement expected (2.2/4.0, SD 0.5, 1.08-3.3). The inter- (0.5-0.7) and intra-observer (0.63-0.79) agreement of the cosmesis was moderate to good, however, poor regarding the recommended reconstruction techniques (mainly  $< 0.50$ ).

**Conclusion** Cosmetic outcome after BCT is influenced by breast and tumour size and ALND. Although several reconstructive options are available, the optimal method for revision surgery has not yet been determined. Future studies are necessary to obtain evidence-based guidelines for reconstructive surgery after BCT.

## INTRODUCTION

Breast cancer surgery has changed dramatically over the past few decades. Breast-conserving therapy (BCT) was introduced in the 1970s as an alternative for the Halsted radical mastectomy, and refers to breast conserving surgery (BCS) in all cases followed by radiotherapy. Several trials demonstrated that BCT yields survival rates comparable to those achieved with mastectomy alone, and therefore BCT has become the standard of care for early-stage breast cancer.<sup>1-3</sup> The main advantage of BCT is preservation of the breast and saving healthy breast tissue, resulting in an improved patient satisfaction compared with mastectomy.<sup>4</sup> However, studies consistently show unsatisfactory cosmetic outcomes in up to 40% of all patients, depending on patient- and tumour characteristics, with large excision volumes being a major contributor to a poor cosmetic outcome.<sup>5-8</sup> A poor cosmetic outcome is mostly described as pronounced breast asymmetry, changed shape of the breast, nipple displacement, scar retraction and skin alterations.<sup>7-12</sup> Poor cosmetic results have a large impact on body image, responsible for lower self-esteem, impaired feelings of sexuality, and depression. Therefore, focusing on the best achievable cosmetic result will most likely lead to a decrease in psychological distress, and improve quality of life after surgery for breast cancer.<sup>13-18</sup>

Although many reconstructive treatment options are available for BCS, such as standard BCS, immediate oncoplastic surgery, or mastectomy with (delayed) reconstruction, limited number of studies are performed to investigate the differences in oncological and cosmetic outcome. Moreover, due to differences in methods to evaluate the cosmetic result, it is difficult to compare the available literature. At length, there is still no consensus regarding the optimal reconstructive technique.<sup>19</sup> The decision as to which delayed reconstruction technique should be used depends on a variety of factors such as the size and shape of the breast, the availability of tissues around the breast and at other sites, and the effects of radiotherapy on breast parenchyma. It is fairly unknown which patient and tumour characteristics are amenable to delayed reconstruction, and subsequently which technique should be used.<sup>20</sup>

### **Aim of the study**

This study aimed to determine the cosmetic outcome following BCT and identify the influence of patient and tumour factors on the cosmesis. Fur-

thermore, we aimed to determine the inter- and intra-observer agreement of breast reconstructive surgeons when choosing their preferred technique for delayed reconstruction.

## **METHODS**

### **Patients**

In total 109 patients were included in this study. All patients underwent BCT for T1-T2 invasive breast cancer. Exclusion criteria were previous breast surgery, thoracotomy, and patients who had undergone radiation of the chest region for other malignancies.

The study was performed in accordance with the Declaration of Helsinki, guidelines for Good Clinical Practice and STROBE guidelines.<sup>21</sup> Written informed consent was obtained, and patient-, tumour- and treatment-characteristics were collected from hospital records. Breast surgery consisted of palpation-, wire- or ultrasound guided lumpectomy. The calculated resection ratio (CRR) was determined by comparing the specimen volume to the optimal resection volume as described by Krekel et al.<sup>22</sup> Additional surgical procedures included either a sentinel node procedure (SN) or an axillary lymph node dissection (ALND). All patients received radiation therapy of the whole breast and a radiotherapy boost to the tumour bed, according to formerly applicable Dutch guidelines and determined by a multidisciplinary team of breast cancer experts. The breast cup-sizes were determined by the authors (V.L.N., J.H.V., N.M.A.K., M.P.v.d.T.) based on the photographs and rated as A/B C/D and > E.

### **Photographs**

Digital frontal photographs of the breasts including the suprasternal notch were taken. Patients were photographed in supine position by one photographer and compiled into a power point presentation.

### **Cosmetic evaluation and reconstructive options**

All photographs were evaluated by four dedicated reconstructive breast surgeons with at least 10 years of experience with breast reconstructive surgery. The cosmetic outcome of the affected breast was evaluated by each surgeon independently with a questionnaire on seven items: I. Shape; II. Volume; III. Deformity; IV. Nipple position; V. Scar; VI. Skin VII. Overall cosmetic result. All items were scored using a 4-point Likert scale

or Harvard scale from excellent, good, fair to poor. For a detailed description of the methods, we refer to Haloua et al.<sup>23</sup>

Furthermore, the surgeons gave their opinion on options for delayed reconstruction on all 7 items. The surgeons were asked whether they would perform reconstructive surgery to improve the cosmetic result of the breasts if the patient would ask for it. This includes the possibility of a patient already scoring 'good' or 'perfect' on cosmesis could also be improved in some cases. It should be mentioned that none of the patients asked for reconstructive surgery and did not receive reconstructive surgery at the time of the evaluation.

The surgeons also indicated how much improvement they expected (4-point Likert scale), and which reconstruction method they preferred. Reported reconstructive options were divided into four groups; flap reconstruction including local transposition flap, latissimus dorsi flap (LD-flap), thoracodorsal artery perforator flap (TAP), deep inferior epigastric perforator (DIEP), either with or without previous ablation. The second group included breast reduction, mastopexy or reconstruction with prosthesis, the third group included lipofilling or liposuction and the fourth group included revision of the scar or nipple reconstruction. Recommended reconstruction techniques were scored by each surgeon.

The cosmetic outcome of the operated breast and expected amount of improvement were correlated to patient and tumour characteristics including age (years), BMI ( $\text{kg}/\text{m}^2$ ), bra cup-size (AB, CD or EFG), palpable versus non palpable tumour, tumour size (cm), excision volume (cc), location of the tumour (upper outer quadrant (UOQ), lower outer quadrant (LOQ), upper inner quadrant (UIQ), lower inner quadrant (LIQ) and periareolar), radiotherapy boost administration, and type of axillary surgery (SN or ALND). Excision volume based on the formula  $(4/3 \pi a b c)$ , with  $a = 1/2$  length,  $b = 1/2$  width and  $c = 1/2$  height as given in the pathology report) previously described by Krekel et al.<sup>22</sup> or as mentioned in the pathology report.

Twenty randomly selected photographs (not included in the current study) were shown to the surgeon's before scoring the photographs of the study population in order to avoid skewness between observations. Intraobserver agreement was tested in a randomly selected set of 50 photographs which have been shown twice during the same session. Interobserver agreement was tested by comparing the results of all the 109 pho-

tos between different surgeons. Intraobserver agreement was tested in a randomly selected set of 50 photographs which have been shown twice during the same session.

### Statistical analysis

All data were analysed by using SPSS, version 22.0. The sum of the cosmetic outcome (factor VIII) was calculated by dividing the sum of the evaluation of the shape, volume, deformity, nipple position, scar and skin (factors I-VI) through 6. The outcome measurements (factors I-VIII) were dichotomized into good (perfect and good; 1-2.4) or poor (fair and poor; 2.5-4). The total sum and overall cosmetic outcome of the four surgeons were averaged. Univariate logistic regression analysis was performed to determine the influence of the patient and tumour characteristics on the mean overall cosmetic outcome of the four surgeons. The linearity assumption of the relation between continuous independent variables and the dependent variable was checked by examining if adding the continuous variable as a categorical variable to the model improved the model significantly. This was not the case for any of the continuous variables so they were included in the models as continuous variables. Subsequently, factors with a p-value below 0.157 were selected for the multivariate logistic regression analysis. The predicted probabilities of the multivariate model were saved and a ROC curve was made with an estimation of the Area Under the Curve (AUC) to assess the discriminative ability of the model to distinguish among patients with a good and poor cosmetic result.<sup>24</sup>

Inter-observer reliability of the seven scores (I-VII) among the four surgeons was tested by calculating Intraclass Correlation Coefficients (ICCs) using a two-way random effects model for absolute agreement. Intra-observer agreement was calculated by dividing the variance between patients ( $\sigma_p^2$ ) and the interaction of the variance between patients and observers ( $\sigma_{po}^2$ ) by the variance between patients ( $\sigma_p^2$ ), the interaction of the variance between patients and observers ( $\sigma_{po}^2$ ), the interaction of the variance between patients and measurements ( $\sigma_{pm}^2$ ) and the error variance ( $\sigma_{residual}^2$ ) (formula 1). An ICC of > 0.7 was considered to indicate a good reliability.<sup>25,26</sup>

$$\text{Intra-observer reliability} = \frac{\sigma_p^2 + \sigma_{po}^2}{\sigma_p^2 + \sigma_{po}^2 + \sigma_{pm}^2 + \sigma_{residual}^2}$$

Formula 1

Characteristics	Median (Min - Max) or percentage
Patient age at operation	57.0 (36-83)
Body mass index (kg/m <sup>2</sup> )	25.5 (17.8-47.8) (n = 96)
Breast size	
A/B	34.9% (n = 38)
C/D	49.5% (n = 54)
E/F/G	15.6% (n = 17)
Tumour size (cm)	1.5 (0.3-5.5) (n = 107)
Type of carcinoma	
Ductal	85.3% (n = 93)
Lobular	4.6% (n = 5)
DCIS	2.8% (n = 3)
Other	8.3% (n = 9)
Tumour location*	
UOQ	53% (n = 58)
LOQ	15% (n = 17)
UIQ	22% (n = 24)
LIQ	5% (n = 5)
Periareolar	4% (n = 4)
Missing	1% (n = 1)
Palpable tumour	
Non-palpable	34% (n = 37)
Palpable	66% (n = 72)
Type of surgery	
Palpation-guided surgery	59% (n = 64)
Wire-guided lumpectomy	15% (n = 17)
Ultrasound-guided surgery	26% (n = 28)
Excision volume (cm <sup>3</sup> )	62,8 (1,0 – 204,2) (n = 94)
CRR	2.55 (0.04 – 16.12) (n = 91)
Axillary surgery	
Sentinel node procedure	67% (n = 73)
Axillary lymph node dissection (ALND)	33% (n = 36)
Boost radiotherapy	84% (n = 92)
Re-excision for tumour-involved margins	17.4% (n = 19)
* UOQ (upper outer quadrant), LOQ (lower outer quadrant), UIQ (upper inner quadrant), LIQ (lower inner quadrant)	

**Table 1** Patient and tumour characteristics and primary outcomes

## RESULTS

### Patient and tumour characteristics

The average age of the included patients was 57.0 years (range 36-83) at the time of surgery, with a median follow-up time of 40 (range 6-172) months. The mean tumour size was 1.5 cm (0.3-5.5), with most tumours being invasive ductal carcinoma (85%). Tumours were mainly located in the UOQ (53%). Standard BCS was performed in all patients, by using either palpation-guided, ultrasound-guided, or wire-guided surgery (59%, 26%, and 15%, respectively). Mean excision volume was 62,8 cm<sup>2</sup> (1,0-204,2). All patients received radiotherapy, a radiotherapy boost was administered in 84% of patients (n = 92) and 33% (n = 36) of the patients underwent ALND (Table 1).

### Cosmetic outcome

The mean sum of the cosmetic outcome (items I-VI) among the four plastic surgeons of the operated breast based on shape, volume, deformity, position of nipple, scar and skin was good (2.4 on a scale of 1-4, SD 0.7, 1.0-4.0). A good score was obtained in 56.9% (n = 62) of patients. The mean overall cosmetic outcome (item VII) was rated as fair (2.7, SD 0,9, 1.0-4.0). A good score was obtained in 49.6% (n = 54) of patients. A reasonable improvement (2,2, SD 0.5, 1.08-3.3) by delayed reconstruction was expected (Table 2).

	Score	% (N)
Cosmetic outcome – specific*	Perfect / good	56.9% (n = 62)
	Fair / poor	43.1% (n = 47)
Overall cosmetic outcome	Perfect / good	49.6% (n = 54)
	Fair / poor	50.5% (n = 55)
Expected improvement**	Significant / reasonable	74.4% (n = 61)
	Minimal / none	25.6% (n = 21)

\* Based on shape, volume, deformity, position of nipple, scar and skin. \*\* Expected improvement if a reconstruction was recommended by one or more surgeons (see Table 4).

**Table 2** Current specific and overall cosmetic outcome and expected improvement of the operated breast

	Univariate model		Multivariate model*	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (years)	1.02 (0.98 – 1.05)	0.417		
Body mass index (kg/m <sup>2</sup> )	1.08 (0.98 – 1.2)	0.130		
Breast size				
A/B	1 (Ref)		1 (Ref)	
C/D	1.78 (0.77 – 4.13)	0.180	1.86 (0.75 – 4.64)	0.183
E/F/G	2.81 (0.86 – 9.23)	0.088	3.81 (1.07 – 13.62)	0.040
Tumour size (cm)	1.63 (1.06 – 2.52)	0.026	1.63 (1.06 – 2.52)	0.028
Tumour location**				
UOQ	1 (Ref)	0.193		
LOQ	2.11 (0.69 – 6.46)	0.184		
UIQ	0.97 (0.37 – 2.52)	0.894		
LIQ	4.59 (0.48 – 43.63)	0.953		
Periareolar	1.15 (0.15 – 8.7)	0.600		
Palpable tumour				
Non-palpable	1 (Ref)			
Palpable	1.12 (0.51 – 2.47)	0.79		
Type of surgery				
Palpation-guided surgery	1 (Ref)			
Wire-guided lumpectomy	1.13 (0.39 – 3.28)	0.829		
Ultrasound-guided surgery	1.00 (0.41 – 2.43)	1.00		
Excision volume (cm <sup>3</sup> )	1.01 (1.00 – 1.02)	0.042		
Boost radiotherapy	1.27 (0.50 – 3.21)	0.619		
Axillary surgery				
Sentinel node procedure	1 (Ref)	1 (Ref)		
Axillary lymph node dissection (ALND)	3.26 (1.39 – 7.61)	0.006	3.09 (1.27 – 7.52)	0.013

\* Only variables with a p-value of < 0.157 were included in the multivariate analysis. \*\* UOQ (upper outer quadrant), LOQ (lower outer quadrant), UIQ (upper inner quadrant), LIQ (lower inner quadrant).

**Table 3** Influencing factors on the cosmetic outcome of the surgeon's evaluation after BCT

### Factors influencing cosmetic outcome

A larger breast size (OR 3.81,  $p = 0.040$ ), a larger tumour (OR 1.63,  $p = 0.028$ ) and ALND (OR 3.09,  $p = 0.013$ ) were risk factors for getting a poor overall cosmetic outcome, even after adjusting for age, BMI, palpable tumour, type of surgery, excision volume, quadrant and boost of radiotherapy. The AUC was 0.72 (95% confidence interval 0.63-0.82), therefore no clinical prediction rule could be developed (Table 3).

### Recommendation of reconstruction

Reconstruction of the ipsilateral side was recommended by one or more surgeons in 55.6% ( $n = 30$ ) of the patients with a good total cosmetic outcome and in 94.5% ( $n = 52$ ) of the patients with a poor cosmesis. Reconstruction of the contralateral side was recommended by one or more surgeons in 16,7% ( $n = 9$ ) of the patients with a good cosmetic outcome and in 76.4% ( $n = 42$ ) in patients with a poor cosmetic result (Table 4).

Recommendation of reconstruction (n = 109)	Ipsilateral	Contralateral
<b>Good cosmetic outcome (n = 54)</b>		
4 surgeons	7.4% (n = 4)	7.4% (n = 4)
3 surgeons	16.7% (n = 9)	3.7% (n = 2)
2 surgeons	11.1% (n = 6)	5.6% (n = 3)
1 surgeon	20.4% (n = 11)	0% (n = 0)
0 surgeons	44.4% (n = 24)	83.3% (n = 45)
<b>Poor cosmetic outcome (n = 55)</b>		
4 surgeons	49.1% (n = 27)	45.5% (n = 25)
3 surgeons	27.3% (n = 15)	12.7% (n = 7)
2 surgeons	9.1% (n = 5)	7.3% (n = 4)
1 surgeon	9.1% (n = 5)	10.9% (n = 6)
0 surgeons	5.5% (n = 3)	23.6% (n = 13)

**Table 4** Recommendation of a reconstruction of the operated (ipsilateral) and contralateral breast after breast conserving therapy

## Recommended reconstruction techniques of the ipsilateral and contralateral breast

In patients with a good cosmetic result, flap reconstruction was suggested in 0.5% of all patients (n = 2), breast reduction, mastopexy or reconstruction with prosthesis in 2.1% (n = 9), lipofilling or liposuction in 9.2% (n = 40) and revision of the scar of nipple reconstruction 3.2% (n = 14).

Flap reconstruction in patients with a poor cosmetic outcome was recommended in 12.4% (n = 54), breast reconstruction in 7.1% (n = 31), lipofilling/suction in 8.5% (n = 37) and scar/nipple surgery 10.6% (n = 46). Reconstruction of the contralateral breast consisted of 13.5% (n = 59) breast reconstruction and 1.1% (n = 5) lipofilling/suction in case of a good cosmesis and 35.3% (n = 154) breast reconstruction in case of a poor cosmesis (Table 5).

Cosmetic outcome	Ipsilateral breast		Contralateral breast	
	Good (n = 54)	Poor (n = 55)	Good (n = 54)	Poor (n = 55)
Overall (n = 436)*				
No reconstruction	34.6% (n = 151)	11.9% (n = 52)	34.9% (n = 152)	15.1% (n = 66)
Flap**	0.5% (n = 2)	12.4% (n = 54)	0.0% (n = 0)	0.0% (n = 0)
Breast***	2.1% (n = 9)	7.1% (n = 31)	13.5% (n = 59)	35.3% (n = 154)
Lipo****	9.2% (n = 40)	8.5% (n = 37)	1.1% (n = 5)	0.0% (n = 0)
Scar/nipple*****	3.2% (n = 14)	10.6% (n = 46)	0.0% (n = 0)	0.0% (n = 0)

\* Total reported reconstruction options by 4 surgeons regarding 109 patients. \*\* Flap reconstruction including local transposition flap, LD (latissimus dorsi) flap, TAP (thoraco-dorsal artery perforator) flap, DIEP (deep inferior epigastric perforator) flap with or without previous ablatio. \*\*\* Breast reduction, mastopexy or reconstruction with prosthesis. \*\*\*\* Lipofilling, liposuction. \*\*\*\*\* Revision scar, nipple reconstruction.

**Table 5** Recommended reconstruction technique in patients with a good (n = 54) or poor (n = 55) cosmetic outcome on operated breast

## Inter-observer agreement

The cosmetic evaluation was comparable between the surgeons, with an inter-observer agreement ranging from 0.50 (0.40-0.60) to 0.70 (0.63-0.77) across the seven cosmetic outcomes. Inter-observer agreement for the recommendation of reconstruction was 0.50 (0.41-0.60). The expected improvement varied among the surgeons with an inter-observer agreement ranging from 0.09 (0.0-0.23) to 0.31 (0.16-0.47).

The intra-observer agreement of the cosmetic evaluation and recommendation of a reconstruction was found to be moderate to good (0.63-0.79) with 62.5% of the ICCs > 0.70. The intra-observer agreement of the reconstruction technique and expected improvement was lower (0.33-0.76), with only 10% of the ICCs > 0.70 (Table 6).

Component	Inter-observer variability (95% CI)	Intra-observer variability (range)
Current shape	0.59 (0.50 – 0.68)	0.66 (0.62; 0.89)
Current volume	0.61 (0.53 – 0.70)	0.79 (0.74; 0.82)
Current deformity	0.63 (0.55 – 0.71)	0.74 (0.61; 0.83)
Current position nipple	0.63 (0.54 – 0.71)	0.69 (0.17; 0.71)
Current scar	0.50 (0.40 – 0.60)	0.64 (0.54; 0.64)
Current skin	0.51 (0.38 – 0.63)	0.76 (0.38; 0.83)
Overall cosmetic outcome	0.70 (0.63 – 0.77)	0.77 (0.74; 0.88)
Recommended reconstruction	0.50 (0.41 – 0.60)	0.78 (0.75; 1.0)
Reconstruction technique	0.39 (0.21 – 0.59)	0.58 (0.0; 0.63)
Contralateral recommended reconstruction	0.45 (0.29 – 0.60)	0.63 (X; 0.64)
Reconstruction technique contralateral	0.53 (0.35 – 0.71)	0.76 (X; 1.0)
Expected improvement shape	0.21 (0.08 – 0.36)	0.62 (0.0; 0.72)
Expected improvement volume	0.31 (0.16 – 0.47)	0.69 (0.0; 1.0)
Expected improvement deformity	0.09 (0.0 – 0.23)	0.33 (0.0; 0.60)
Expected improvement position nipple	0.21 (0.08 – 0.37)	0.34 (0.0; 0.75)
Expected improvement scar	0.20 (0.08 – 0.36)	0.69 (0.0; 0.69)
Expected improvement skin	0.19 (0.08 – 0.36)	0.54 (0.0; 0.57)
Expected improvement overall	0.24 (0.11 – 0.40)	0.43 (0.46; 1.0)

X Scale has zero variance items (ICC could therefore not be calculated).

**Table 6** Inter- and intra-observer variability of the assessment of the current cosmetic outcome, recommended reconstruction techniques and expected improvement after BCT

## DISCUSSION

### Cosmetic outcome

BCT is now considered as the standard surgical procedure for early stage breast cancer for which it has shown to be equivalent to mastectomy with regard to oncological outcome.<sup>1-3</sup> In this cohort, four reconstructive surgeons rated the cosmetic outcome following BCT in 109 patients on average as fair (2.7 on a scale from 1 to 4, SD 0.9). In 50.5% of the patients the cosmetic results were rated fair to poor, which is a higher rate than the 40% poor cosmesis that is reported in the literature.<sup>5-8</sup>

Matory et al also found a high percentage of poor cosmetic outcome after BCS.<sup>11</sup> They evaluated the result of 57 patients after BCT by comparing the patient evaluation, radiotherapist, surgeon and plastic surgeon assessment. The patients, radiotherapist and surgeon rated the cosmesis as good or excellent in over 80% of the patients, while the plastic surgeon reported only 50% good cosmesis.<sup>11</sup> Possibly, plastic, and reconstructive surgeons are more strict in evaluating cosmetic outcomes, which could be due to their focus on the reconstructive part of the procedure instead of the oncological treatment. The evaluation of the surgeon has proven to be a valuable method for the cosmetic evaluation after BCT,<sup>27</sup> but a surgeon assessment brings up some difficulties as well.<sup>28</sup> For example, professionals may be more biased in their expert opinion than non-professionals due to their (own) results achieved, and cosmetic experts, such as plastic and reconstructive surgeons, will presumably focus on different items than non-professionals, surgical residents, breast surgeons or the patient herself. Haloua et al reported a moderate to substantial agreement between non-professionals, breast surgeons and plastic surgeons.<sup>23</sup>

The final cosmetic results and the options for breast reconstruction should preferably be discussed in a multidisciplinary team in collaboration with the oncological and plastic surgeon. However, the patient's demand for a secondary correction of the breast(s) is obviously leading in the final decision for reconstructive surgery following BCT. This study consists of expert opinions only, which differ from patient reported outcomes. As their own evaluation of the cosmetic outcome better reflects quality of life, future studies should also focus on patient reported outcomes and patients' demands for a secondary reconstruction.<sup>18, 29</sup>

### **Factors influencing cosmetic outcome**

Risk factors for a poor cosmetic result in this cohort were evaluated; a larger breast size (OR 3.81,  $p = 0.040$ ), a larger tumour (OR 1.63,  $p = 0.028$ ) and ALND (OR 3.09,  $p = 0.013$ ) were indicated as important independent predictors of a poor overall cosmetic outcome, after adjusting for patient and tumour characteristics. In the literature several factors influencing the cosmetic outcome are known, such as younger age, lower BMI, larger tumour size and retroareolar location of the tumour, radiotherapy, chemotherapy and ALND.<sup>5, 8, 30</sup> The influence of the size of the breast on the cosmetic outcome is debatable, whereas studies report both positive and negative effects of small breast size on the cosmesis.<sup>8, 31</sup> Larger breast sizes are at risk for a poor cosmetic outcome. Moody et al reported possible greater radiation changes that result from greater dose inhomogeneity in women with larger breasts.<sup>32</sup>

In this cohort, 33% ( $n = 36$ ) of the patients underwent ALND. Since the Z0011 trial of Guiliano et al this percentage has decreased dramatically.<sup>33</sup> Patients undergoing ALND or having large tumours should be informed before the surgery that they are at risk for having a poor cosmetic outcome. As all patients in this study received whole breast radiation therapy, no significant effect on the cosmesis could be indicated. However, no influence on the cosmetic outcome was found of the radiotherapy boost to the tumour bed (84% ( $n = 92$ ) of the patients (OR 1.27,  $p = 0.619$ ). In the “boost versus no boost” trial a significant effect of a radiotherapy boost has been shown.<sup>34</sup> This was not confirmed in our study, which might be due to the small number of patients without a radiotherapy boost (16%,  $n = 17$ ). Although the tumour size was relatively small (1.5 cm, range 0.3-5.5), the final cosmetic result was rather poor. If the patient would ask for a correction, there are several reconstructive surgical options to improve the cosmetic outcome.

### **Reconstructive options**

Ipsilateral reconstruction techniques in this cohort consisted mainly of flap reconstruction, revision of the scar or nipple reconstruction and lipofilling or liposuction. There are studies reporting on the different reconstruction methods, but the evidence is limited.<sup>19, 20, 35</sup> The choice for type of reconstruction is mainly based on the experience of the surgeon and differs between one and another.<sup>20</sup> A promising technique is autologous fat grafting or lipofilling. Lipofilling is a noninvasive procedure that results in minimal scarring. Although tissue augmentation by lipofilling does have

several advantages, it is essential that such a procedure is supported by evidence-based medicine and that further basic scientific and clinical research is conducted to ensure that lipofilling is a safe and effective procedure at the long term.<sup>36, 37</sup> The most commonly advised reconstructive technique of the contralateral side in this cohort was a breast reduction and mastopexy. Breast reduction is known to be a good option for symmetrizing the cosmetic result after BCT.<sup>38</sup> This can however only be offered to patients who possess enough tissue to undergo reduction and a breast with sufficient volume will remain.

### **Inter- and intraobserver agreement**

The inter- (0.5-0.7) and intraobserver (0.63-0.79) agreement of the cosmetic outcome was moderate to good. However, the inter- and intraobserver agreement of the recommended reconstruction techniques and expected improvements was mainly  $< 0.70$ , which implies high variance between and within raters, explaining the variety in reconstruction options.

The intra-observer agreement was based on photographs that were shown twice during the same session. Different results may have been found when the surgeons would have looked at the patients themselves twice instead of the photographs. Moreover, in order to avoid rating of the results based on memory, these measurements should preferably be done at different time points.

At length the AUC was insufficiently high to develop a clinical prediction rule (0.72; 0.63-0.82). More research should be done in larger studies in order to develop a proper prediction model for the cosmetic outcome after BCT, thereby providing a clear and objective advice regarding the optimal reconstruction method.

The cosmetic outcome after BCT can still benefit from improvement. Larger breast size, larger tumour size and ALND are risk factors for a poor cosmesis. In patients with a poor cosmetic result, surgical intervention is recommended in up to 95% for the ipsilateral breast and in 76% for the contralateral breast. The assessment of the cosmesis by reconstructive surgeons yields comparable results, but a strong disagreement regarding the reconstruction techniques is present. Currently no method is yet available to determine and advise the best technique for a delayed reconstruction. Future studies should focus on developing the optimal algorithm for reconstructive surgery with the best cosmetic result and thereby obtain evidence-based guidelines for breast reconstruction after BCT.

## REFERENCES

1. Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med.* 2002;347(16):1233-41.
2. Veronesi U, Banfi A, Salvadori B, et al. Breast conservation is the treatment of choice in small breast cancer: Long-term results of a randomized trial. *Eur J Cancer.* 1990;26(6):668-70.
3. Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med.* 2002;347(16):1227-32.
4. Jagsi R, Li Y, Morrow M, et al. Patient-reported Quality of Life and Satisfaction With Cosmetic Outcomes After Breast Conservation and Mastectomy With and Without Reconstruction: Results of a Survey of Breast Cancer Survivors. *Ann Surg.* 2015;261(6):1198-206.
5. Ozmen T, Polat AV, Polat AK, et al. Factors affecting cosmesis after breast conserving surgery without oncoplastic techniques in an experienced comprehensive breast center. *The Surgeon.* 2015;13(3):139-44.
6. Chan SW, Cheung PS, Lam SH. Cosmetic outcome and percentage of breast volume excision in oncoplastic breast conserving surgery. *World J Surg.* 2010;34(7):1447-52.
7. Sneeuw KCA, Aaronson NK, Yarnold JR, et al. Cosmetic and functional outcomes of breast conserving treatment for early stage breast cancer. 1. Comparison of patients' ratings, observers' ratings and objective assessments. *Radiother Oncol.* 1992;25:153-59.
8. Al-Ghazal SK, Blamey RW, Stewart J, et al. The cosmetic outcome in early breast cancer treated with breast conservation. *Eur J Surg Oncol.* 1999;25(566-570).
9. Taylor ME, Perez CA, Halverson KJ, et al. Factors influencing cosmetic results after conservation therapy for breast cancer. *Int J Radiation Oncol Biol Phys.* 1995;31(4):753-64.
10. Van Limbergen E, Rijnders A, van der Schueren E, et al. Cosmetic evaluation of breast conserving treatment for mammary cancer. 2. A quantitative analysis of the influence of radiation dose, fractionation schedules and surgical treatment techniques on cosmetic results. *Radiother Oncol.* 1989;16:253-67.
11. Matory WEJ, Wertheimer M, Fitzgerald TJ, et al. Aesthetic results following partial mastectomy and radiation therapy. *Plast Reconstr Surg.* 1990;85:739-46.
12. Berrino P, Campora A, Leone S, et al. Correction of type II breast deformities following conservative cancer surgery. *Plast Reconstr Surg.* 1992;90(846-853).
13. Al-Ghazal SK, Fallowfield L, Blamey RW. Does cosmetic outcome from treatment of primary breast cancer influence psychosocial morbidity? *Eur J Surg Oncol.* 1999;25:571-73.
14. Curran D, van Dongen JP, Aaronson NK, et al. Quality of life of early-stage breast cancer patients treated with radical mastectomy or breast-conserving procedures: results of EORTC trial 10801. *Eur J Cancer.* 1998;34(3):307-14.
15. Sneeuw KCA, Aaronson NK, Yarnold JR, et al. Cosmetic and functional outcomes of breast conserving treatment for early stage breast cancer. 2. Relationship with psychosocial functioning. *Radiother Oncol.* 1992;25:160-66.
16. Waljee JF, Hu ES, Ubel PA, et al. Effect of Esthetic Outcome After Breast-Conserving Surgery on Psychosocial Functioning and Quality of Life. *J Clin Oncol.* 2008;26(20):3331-37.
17. Hau E, Browne L, Capp A, et al. The impact of breast cosmetic and functional outcomes on quality of life: long-term results from the St. George and Wollongong randomized breast boost trial. *Breast Cancer Res Treat.* 2013;139(1):115-23.

18. Kim MK, Kim T, Moon HG, et al. Effect of cosmetic outcome on quality of life after breast cancer surgery. *Eur J Surg Oncol.* 2015;41(3):426-32.
19. Haloua MH, Krekel NMA, Winters HAH, et al. A Systematic Review of Oncoplastic Breast-Conserving Surgery. *Annals of Surgery.* 2013;257(4):609-20.
20. Munhoz AM, Montag E, Filassi JR, et al. Current approaches to managing partial breast defects: the role of conservative breast surgery reconstruction. *Anticancer Res.* 2014;34(3):1099-114.
21. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet.* 2007;370(9596):1453-7.
22. Krekel NMA, Zonderhuis BM, Schreurs HWH, et al. Ultrasound-guided breast-sparing surgery to improve cosmetic outcomes and quality of life. A prospective multicentre randomised controlled clinical trial comparing ultrasound-guided surgery to traditional palpation-guided surgery (COBALT trial). *BMC Surg.* 2011;11(1):8.
23. Haloua MH, Krekel NMA, Jacobs GJA, et al. Cosmetic Outcome Assessment following Breast-Conserving Therapy: A Comparison between BCCT.core Software and Panel Evaluation. *Int J Breast Cancer.* 2014;2014:1-7.
24. Schellingerhout JM, Heymans MW, de Vet HC, et al. Categorizing continuous variables resulted in different predictors in a prognostic model for nonspecific neck pain. *J Clin Epidemiol.* 2009;62(8):868-74.
25. Streiner DL, Norman GR. Health measurement scales - A practical guide to their development and use. 4 ed. Oxford, UK: Oxford University Press; 2008.
26. de Vet HCW, Terwee CB, Mokkink LB, et al. Measurement in Medicine: A Practive Guide: Cambridge University Press; 2011.
27. Vrieling C, Collette L, Fourquet A, et al. The influence of patient, tumor and treatment factors on the cosmetic results after breast-conserving therapy in the EORTC 'boost vs. no boost' trial. EORTC Radiotherapy and Breast Cancer Cooperative Groups. *Radiother Oncol.* 2000;55(3):219-32.
28. Cardoso MJ, Oliveira H, Cardoso J. Assessing cosmetic results after breast conserving surgery. *J Surg Oncol.* 2014;110(1):37-44.
29. Volders JH, Haloua MH, Krekel NM, et al. Intraoperative ultrasound guidance in breast-conserving surgery shows superiority in oncological outcome, long-term cosmetic and patient-reported outcomes: Final outcomes of a randomized controlled trial (COBALT). *Eur J Surg Oncol.* 2016.
30. Hennigs A, Hartmann B, Rauch G, et al. Long-term objective esthetic outcome after breast-conserving therapy. *Breast Cancer Res Treat.* 2015;153(2):345-51.
31. Lyngholm CD, Christiansen PM, Damsgaard TE, et al. Long-term follow-up of late morbidity, cosmetic outcome and body image after breast conserving therapy. A study from the Danish Breast Cancer Cooperative Group (DBCG). *Acta Oncol.* 2013;52:259-69.
32. Moody AM, Mayles WP, Bliss JM, et al. The influence of breast size on late radiation effects and association with radiotherapy dose inhomogeneity. *Radiother Oncol.* 1994;33(2):106-12.
33. Giuliano AE, Hunt KK, Ballman KV, et al. Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial. *JAMA.* 2011;305(6):569-75.
34. Vrieling C, Collette L, Fourquet A, et al. The influence of the boost in breast-conserving therapy on cosmetic outcome in the EORTC "boost versus no boost" trial. EORTC Radiotherapy and Breast Cancer Cooperative Groups. European Organization for Research and Treatment of Cancer. *Int J Radiat Oncol Biol Phys.* 1999;45(3):677-85.

35. D'Souza N, Darmanin G, Fedorowicz Z. Immediate versus delayed reconstruction following surgery for breast cancer. *Cochrane Database Syst Rev*. 2011(7):CD008674. DOI: 10.1002/14651858.CD008674.pub2.
36. Agha RA, Fowler AJ, Herlin C, et al. Use of autologous fat grafting for breast reconstruction: a systematic review with meta-analysis of oncological outcomes. *J Plast Reconstr Aesthet Surg*. 2015;68(2):143-61.
37. Groen JW, Negenborn VL, Twisk DJ, et al. Autologous fat grafting in onco-plastic breast reconstruction: A systematic review on oncological and radiological safety, complications, volume retention and patient/surgeon satisfaction. *J Plast Reconstr Aesthet Surg*. 2016;69(6):742-64.
38. Kronowitz SJ, Feledy JA, Hunt KK, et al. Determining the Optimal Approach to Breast Reconstruction after Partial Mastectomy. *Plast Reconstr Surg*. 2006;117(1):1-11.